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A REVIEW OF THE MEDICINAL VALUES, PHARMACOLOGICAL ACTIONS, MORPHOLOGICAL EFFECTS AND TOXICITY OF *OCIMUM GRATISSIMUM* LINN

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ABSTRACT

Herbal medicine is the oldest form of health care known to mankind and herbs have been used by all cultures throughout history, as such it is an integral part of the development of modern civilization. *Ocimum gratissimum* (OG) Linn belongs to the family Lamiaceae and found mostly in the savannah and coastal areas of tropical countries, including Nigeria, India, Mexico and Brazil. *Ocimum gratissimum* leaves have attracted considerable attention from researchers because of their extensive medicinal value, culinary use and pharmacological actions. The plant is used by ethnomedical practitioners in the treatment of epilepsy, high fever and diarrhoea, fungal infections, fever, cold and catarrh, while in the Savannah areas, decoctions of the leaves are used to treat mental illness and management of the baby's umbilical cord, to keep the wound surfaces sterile. The essential oils from the leaves and flowers of OG have been used in the preparation of teas, infusions and incorporated in a variety of bases as topical antiseptics and for use in the treatment of minor wounds, boils and pimples. The anti-inflammatory, analgesic, wound healing, antimicrobial, antioxidant, diaphoretic, antipyretic, antiseptic, antitussive and antispasmodic activities of OG have been reported. However, despite of the high medicinal benefits and pharmacological activities of OG, the essential oil from OG is capable of invoking an inflammatory response on persistent administration, hence, the toxic potentials and morphological effects of the plant should not be overlooked. This review consisting of references from literature search of journals, using different search engines and chapters in books aims at highlighting the medicinal values, pharmacological actions, morphological effects and toxicity of *Ocimum gratissimum*.

KEYWORDS: Herbal medicine, *Ocimum gratissimum*, toxicity, pharmacological activity, morphological effects.

INTRODUCTION

Ocimum gratissimum (OG), one of the over 50 species of herbs and shrubs known in Africa as 'Scent leaf' and in Taiwan as 'Chit-Chan-Than,[1] from the genius *Ocimum*, belongs to the family Lamiaceae and found mostly in the tropical countries, including Nigeria, India, North and South America, Mexico and Brazil.[2,3] The plant is indigenous to tropical areas especially India and West Africa. It is also found in the savannah and coastal areas and cultivated in Sri Lanka, South Sea Islands, and also within Nepal, Bengal, Chittagong and Deccan.[4] *Ocimum gratissimum* is known by various names in different parts of the world. In India it is known by its several vernacular names, the most commonly used ones being Vriddhutulsi (Sanskrit), Ram tulsi (Hindi), and Nimma tulasi (Kannada). In the southern part of Nigeria, the plant is called "effinrin-nla" by the Yoruba speaking tribe. It is called "Ahuji" by the Igbos, while in the Northern part of Nigeria, the Hausas call it "Daidoya".[5] *Ocimum gratissimum* has been used extensively in the traditional system of medicine in many countries.

Ocimum gratissimum is an aromatic, perennial herb, 1-3 m tall; stem erect, round-quadrangular, much branched, glabrous or pubescent, woody at the base, often with epidermis peeling in strips.[6] *Ocimum gratissimum* like most *Ocimum* species contains the essential oil eugenol but it is primarily consumed as a vegetable, as a spice or as medicine.[7,8] When extracts from the leaves of OG were investigated for phytochemical constituent and anti-oxidant activity, tests for tannins, steroids, terpenoids, flavonoids and cardiac glycosides were positive in both methanolic and aqueous extracts.[3]

The nutritional importance of OG centres on its usefulness as a seasoning because of its aromatic flavor.[9] In folk medicine, OG is extensively used throughout West Africa as a febrifuge, anti-malarial, anti-convulsant and against cough.[10] Some phytochemical constituents of OG have been isolated and identified. The volatile aromatic oil from the leaves consists mainly of thymol (32-65%) and eugenol.[9] It also contains xanthones, terpenes and lactone.[11]

Ocimum gratissimum is traditionally used to relieve pains, treatment of rheumatism, diarrhea, high fever, convulsions, diabetes, eczema, piles and as a repellant.[12-14] Extract from the leaves of OG possesses good antioxidant potential presumably because of its phytochemical constituents.[12,15] In the Northeastern part of Brazil, it is used for medicinal, condiment and culinary purposes. The flowers and the leaves of this plant are rich in essential oils so it is used in preparation of teas and infusion.[15] The crushed leaf juice is used in the treatment of convulsion, stomach pain and catarrh. Oil from the leaves has been found to possess antiseptic, anti-bacterial and antifungal activities.[7,10,16,17] In the coastal areas of Nigeria, the plant is used in the treatment of epilepsy, high fever and diarrhoea.[5] In the savannah areas decoctions of the leaves are used to treat mental illness.[3] *Ocimum gratissimum* is used by the Ibos of Southeastern Nigeria in the management of baby's cord, to keep the wound surfaces sterile. It is also used in the treatment of fungal infections, fever, cold and catarrh.[8] Phytochemical evaluation of this plant has shown that it is rich in alkaloid, saponin, tannin, phytates, flavonoids and oligosaccharides and contains tolerable gyanogenic substances.[18] The plant is also said to contain major mineral elements like calcium, chloride, manganese, magnesium, zinc and potassium.[19] In spite of the high medicinal benefits and pharmacological activities of OG, the *Ocimum* oil is capable of invoking an inflammatory response on persistent administration, hence, the toxic potentials and morphological effects of the plant should not be overlooked. This review consisting of references from literature search of journals and chapters in books aims at highlighting the medicinal values, pharmacological actions, morphological effects and toxicityn of *Ocimum gratissimum*.

Taxonomy

Kingdom:	Plantae
Subkingdom:	Tracheobionta
Super division:	Spermatophyta
Division:	Magnoliophyta
Class:	Magnoliopsida
Subclass:	Asteridae
Order:	Lamiales
Family:	Lamiaceae
Genus:	*Ocimum* L.
Species:	*Gratissimum*

Fig 1: Whole plant of *Ocimum gratissimum* with the leaves and flowers (Wikipedia.org).

Compounds isolated from *Ocimum gratissimum* linn

In the past few years, the demand of essential oils derived from almost all parts of aromatic plants has increased due to their importance in native medicine systems.[20] Essential oils extracted from OG have been employed in different biological activities, including, application in perfumery, inhibition of growth of microorganisms, aromatherapy and in food preservation as they have been reported to possess interesting biological properties.[21,22] Numerous researchers have established the biological activities of essential oils from different *Ocimum* species, Pandey *et al*.[23], described some important isolates the essential oils of OG from different parts of the world (Fig 2).

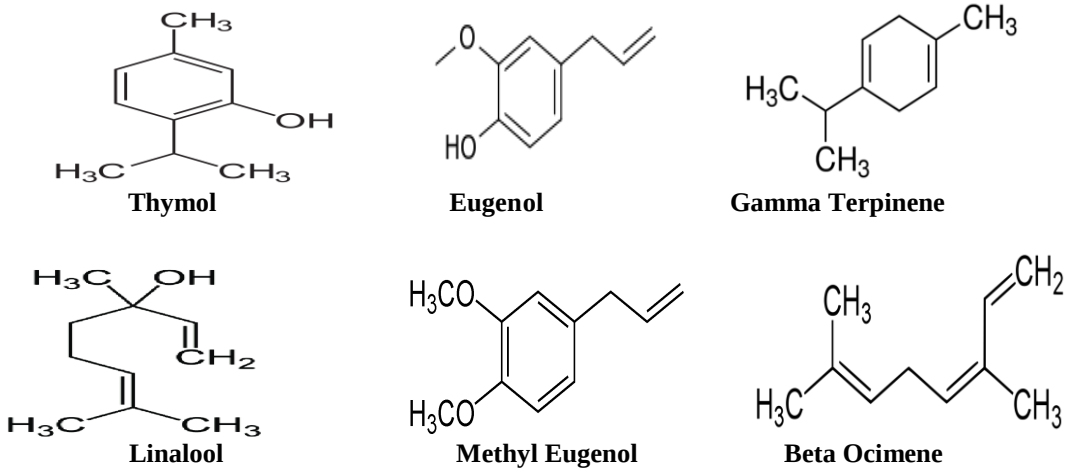

Fig 2: Chemical structures of some compounds isolated from essential oils of *Ocimum gratissimum* (Pandey et al., 2014).[23]

Medicinal/Traditional uses of *Ocimum gratissimum*

In many countries, OG has been extensively used in the traditional system of medicine. Rabelo[15] reported the use of OG for medicinal, condiment and culinary purpose in North east of Brazil, while the essential oils from the leaves and flowers of the plant was used in the preparation of teas and infusion. The root extracts of OG have been used as a decoction by Brazilians in the tropical forest to sedative for children.[24]

In the coastal areas of Nigeria, the plant is used in the treatment of epilepsy, high fever and diarrhoea,[5] while in the Savannah areas, the leaves are used as decoctions to treat mental illness.[3] The Ibos of Southeastern Nigeria uses OG in the management of the baby's umbilical cord, to keep the wound surfaces sterile. It is also used in the treatment of fungal infections, fever, cold and catarrh.[8] Also in Southwestern Nigeria, the leaf extracts of OG is used in the treatment of diarrhoea, while the cold leaf infusions are used for the relief of stomach upset and hemorrhoids.[25] In Nigeria, the plant is used in the treatment of miscarriage[26] and possesses antihelmintic[27] activities.

In Kenya and other sub Saharan African communities, Matasyoh *et al*.[22] reported that OG is used for various purposes, including; the leaves being rubbed between the palms and sniffed as a treatment for blocked nostrils, used for abdominal pains, sore eyes, ear infections, coughs, barrenness, fever, convulsions, and tooth gargle, regulation of menstruation and as a cure for rectal prolapse.

Oliver[28] and Ta'nia *et al*.[29] reported in India, the use of the whole plant for the treatment of headache, influenza and sunstroke, for its anti-inflammatory activity, as a diaphoretic, and antipyretic.

In folkloric medicine, OG has been used in the treatment of different diseases such as diarrhoea, upper respiratory tract infections, diseases of the eye, skin diseases, conjunctivitis, pneumonia, cough, headache, fever,[30] warts, worms, kidney infections and diabetes mellitus.[31] Ngassoum *et al*.[32] reported that the infusion of OG leaves is used as pulmonary antiseptic, antitussive and antispasmodic agents.

Pharmacological actions and Morphological effects of *Ocimum gratissimum* on organ/system

Presently there is an increasing interest worldwide in herbal medicines accompanied by increased laboratory investigation into the pharmacological properties of the bioactive ingredients and their ability to treat various diseases.[33] Sofowora[34] reported that the leave extracts of OG plant are used by different tribes for different purposes in West Africa and Nigeria. The pharmacological activities of OG have been reported by various researchers, including; antioxidant activity,[3,35-37] antibacterial activity,[38, 30,39-42] antifungal activity,[43-46] antidiarrhoeal activity,[47-49] antihelmintic activity,[27] antitumor and anti-cancer potentials,[50,51] analgesic activity,[52-54] mosquito-repellent and mosquitocidal potential,[55] antidiabetic property,[56-60] anti-ulcer property,[61] anti-inflammatory property,[62,54,63,64] anti-nociceptive activity,[65] anxiolytic,[54,66] antimutagenic activity,[67,68] antihypertensive property,[69,70] immunostimulatory effect,[71,72] anticonvulsant activity [73,66,54] and nematicidal activity.[74]

The rich phytochemical content and good antioxidant activity of OG have been suggested by researchers to be responsible for its free radical scavenging activity and protection against oxidative stress-induced morphological and cellular damage in several organs/systems,[3] as described below;

Skin/wound healing effect of *Ocimum gratissimum*

Dubey *et al*.[75] suggested that due to the polyvalent performances and the sweet fragrance of the essential oil of OG containing a high level of ethyl cinnamate, it may be suitable for dermatology and cosmetology. One of the characteristic features of normal wound healing is persistent microvascular hyperpermeability to plasma proteins.[76,77] Orafidiya *et al*.[77] reported that increasing vascular permeability in rabbits by the essential oil of OG leaf may be one of the factors contributing to the wound healing property of OG. Osuagwu *et al*.[78] suggested that OG leaf extract could be a potential wound healing agent due to its ability to enhance wound contraction. Orafidiya *et al*.[79] in a preliminary study reported the efficacy of the essential oil of OG leaf in promoting hair growth in cyclophoshamde-induced hair loss by promoting follicular proliferation.

Effects *Ocimum gratissimum* on the respiratory system

Chen *et al*.[80] investigated whether aqueous extract of OG affects viability of A549 cells and the signals induced by OG in A549 cells. Cell viability assays revealed that OG significantly and dose-dependently decreased the viability of A549 cell but not that of BEAS-2B cell. Morphological examination and DAPI staining indicated that OG induced cell shrinkage and DNA condensation for A549 cells. Further investigation showed that OG enhanced activation of caspase-3, caspase-9 and caspase-8 and increased protein level of Apaf-1 and Bak, but diminished the level of Bcl-2. Additionally, OG inhibited the phosphorylation of extracellular signal-regulated kinase (ERK) yet enhanced the phosphorylation of c-Jun N-terminal kinase (JNK) and p38 MAP kinase (p38). They concluded that extracts of OG suppressed the cell viability of A549 cells, which may result from the activation of apoptotic signaling and the inhibition of anti-apoptotic signaling, suggesting that OG might be beneficial to lung carcinoma treatment.

Behbahani[81] reported that eugenol, lutein and lupeol isolated from the essential oil of OG induced p53, decreased expression of bcl-2 and increased expression of BAX proteins to trigger apoptosis in MCF-7 and

MDA-MB-231 cells thereby drawing the importance of eradication of various kinds of cancer in possible ways by OG. The results from the study showed that the aqueous leaf extract of OG suppresses coughing by reducing tracheal fluid secretion in addition to a possible central effect of inhibiting the cough centre. The antisecretory effect may be helpful in chronic asthma. The results lend credence to the ethnomedicinal use of the extract in the treatment of cough and asthma.[82] In addition, nasal administration of thymol (constituent of the essential oil of OG) has been associated with reduction in the urge to cough by olfactory mechanism.[83]

Effects of *Ocimum gratissimum* on the gastro-intestinal tract

Madeira *et al*.[84] reported that the essential oil of OG relaxed the smooth muscles of the small intestine by its direct effect on the smooth muscle of the ileum which may underlie the therapeutic effect of the plant and is consistent with the popular use of the plant to treat gastrointestinal disorders.

Effraim *et al*.[85] reported the hepatoprotective effect of OG and showed that rats treated with 1.6 g/kg of the extract depicted an establishment of the normal structure of the liver, with the hepatocytes showing no sign of oedema, hypertrophy resulting in larger (normal) sinusoidal diameter, indicating the usefulness of OG as a hepatoprotective agent. Akah *et al*.[61] reported the gastro-protective activity of the methanolic extract of OG. In their experiment, the antiulcer effect was evaluated in the guts of guinea pig, rabbit and mice. They showed that OG extract reduced gastrointestinal motility in mice, produced concentration-dependent relaxation of the smooth muscle of the jejunum and inhibited acetylcholine contractile response. They concluded that methanolic extract of OG offers protection against ulcer and could justify the folkloric use of the plant in peptic ulcer diseases.

Essential oils obtained from Ocimum species showed various medicinal potentials in chemopreventive, anticarcinogenic, free radical scavenging, and radioprotective uses.[86-88] Additionally, ethanolic extract of OG leaf also revealed significant chemopreventive effects on chemical-induced papilloma genesis by modulating metabolizing enzymes such as cytochrome P450, glutathione-s-transferase, and aryl hydrocarbon hydroxylase.[89,90] Moreover, a study indicated that administered orally aqueous extract of OG leaf could reduce oxidative and toxicant activity and enhance specific activities of hepatic antioxidant enzymes in rats.[91]

Surana and Jain[92] investigated the hepatoprotective effect of ethanolic extract of OG against carbon tetra chloride (CCL_4)-induced hepatic damage in rats and reported that markers of liver injury, increased aminotransferase, alkaline phosphatase, bilirubin and morphological changes such as necrosis and collagen deposition, were significantly decreased in rats treated with ethanolic extract of OG, suggesting that the OG showed hepatoprotective effect on carbon tetrachloride induced hepatic damage which may be a potential clinical application for treatment of liver diseases.

In another experiment by Chiu *et al*.[93] aqueous extract of OG protected the liver from CCL_4-induced chronic hepatic injury by significantly decreasing stress proteins including heat shock protein (HSP) 70, inducible nitric oxide synthase (iNOS), MMP-9/MMP-2 ratio, uPA, phosphorylated ERK (p-ERK) and NF-κB (p-P65) which was detected in livers of CCl_4-administrated rats. Their findings implied that OGAE can efficiently inhibit CCl4-induced liver injuries in rats and may therefore be a potential food or herb for preventing liver injuries.

Huang *et al*.[94] investigate the effects and inhibitive mechanisms of aqueous extract of OG leaf which is commonly used as a therapeutic herb for its numerous pharmacological properties, on malignant hepatocellular carcinoma (HCC) cells. Their results showed that extracts of OG decreased the cell viability of HCC SK-Hep1 and HA22T cells in a dose-dependent manner (from 400 to 800 μg/mL), with little effect on Chang liver cells. Their findings raise suspicion that the extracts of OG-induced cell death may be mediated through proteins that regulate cell cycle and apoptosis in SK-Hep1 and HA22T cells, and further experimentation revealed that OG treatment resulted in a dose-dependent decrease in caspase 3 and PARP expressions and in CDK4and p-ERK1/2expressions. Animal experiments also exhibited decreased HCC tumor growth by OG treatment. Huang *et al*. [94] therefore suggested that the inhibition of cell viability and tumor growth induced by extracts of OG may be correlated to the alteration of apoptosis-related proteins.

Effect of *Ocimum gratissimum* on the nervous system

Freire *et al*.[95] studied the effect of the eugenol, a type of essential oils isolated from OG on the central nervous system (CNS) by evaluating the open-field and rota-rod tests; sleeping time induced by sodium pentobarbital (PBS, 40 mg/kg, intra-peritoneally, i.p.) and anticonvulsant activity against seizures induced by both pentylenetetrazole (PTZ; 85 mg/kg, s.c.) and maximal electroshock (MES, 50 mA, 0.11 s). They reported that the essential oils effectively increased the sleeping duration and protected the animals against tonic seizures induced by electroshock.

Olayinka *et al*.[96] studied the role of OG in modulating neurodegenerative changes in rats fed with high concentration of Lead (Pb) acetate. They observed high blood Pb levels, increased lipid peroxidation and decreased glutathione levels resulting in neurotoxic changes in the brain tissue in the rats treated with lead acetate. They reported the neurodegenerative modulating effect of OG extract in the group of rats supplemented

with the extract and suggested that, extracts of this plant after proper standardization could be a good supplement in the management of neurodegenerative changes occasioned by excessive Lead ingestion in children with Lead encephalopathy.

Bora *et al*.[97] investigated the potential protective effects of ethanol extract of OG against focal ischemia and reperfusion (I/R) insult in rat brain. Occlusion of the middle cerebral artery (MCA) (used in inducing ischaemia) resulted in increased cerebral infarct volume and lipid peroxidation, and depletion in SOD and GPx in brain. Elevated neurological deficits were also significantly observed by MCA occlusion. They reported that, all the brain oxidative stress, damage and neurological deficits were significantly attenuated by pre-treatment with 150 or 300 mg/kg, p.o., ethanolic extract of OG. They suggested the neuroprotective potential of OG in cerebral ischemia, mediated through its antioxidant activity and as such, OG extracts should be investigated further as a possible strategy against cerebral stroke.

Ibegbu *et al*.[98] studied the biochemical, haematological and morphological effects of ethanolic leaf extract of OG on sodium nitrite ($NaNO_2$)-induced cerebellar toxicity in adult Wistar rats. They reported increased in serum levels of malondialdehyde and a decrease in superoxide dismutase, glutathione peroxidase, and catalase, increased increase in red blood cells, white blood cells, mean corpuscular volume, and mean corpuscular hemoglobin, and degenerative changes in the cerebellar cortex of the rats treated with $NaNO_2$ only. Extracts of OG administered, ameliorated the altered biochemical, haematological and morphological indices and concluded that OG in a controlled manner may be useful in the management of neurodegenerative conditions involving free radical generation and reduction in brain energy production.

Imosemi and Okori[99] investigated the neuroprotective effects of ethanolic leaf extract of OG on monosodium glutamate (MSG)-induced oxidative stress in developing Wistar rat cerebellum and reported decreased GSH, GPx and reduced thickness of the molecular layer of the postnatal developing cerebellar cortex in the rats treated with MSG. Extracts of OG was able to reverse the adverse effect of MSG-neurotoxicity and suggested that OG possesses the bioactive phytochemicals capable of preventing or reversing MSG-induced oxidative stress in the brain.

Chao *et al*.[1] examined the protective effects of aqueous extracts of OG against cell damage caused by H_2O_2-induced oxidative stress in RSC96 Schwann cells. Their results showed that the RSC96 cells, damaged by H_2O_2 oxidative stress, decreased their viability up to 32% after treatment with different concentrations of up to 300 μM H_2O_2, but extracts of OG pretreatment (150 or 200 μg/mL) increased cell viability by approximately 62% or 66%, respectively. Cell cycle analysis indicated a high (43%) sub-G1 cell population in the H_2O_2-treated RSC96 cells compared with untreated cells (1%); whereas OGE pretreatment (150 and 200 μg/mL) of RSC96 cells significantly reduced the sub-G1 cells (7% and 8%, respectively). Also, employing Western blot analysis, they revealed that OG pretreatment inhibited H_2O_2-induced apoptotic protein caspase-3 activation and PARP cleavage, as well as reversal of Bax up-regulation and Bcl-2 down-regulation. The amelioration of cell stress and stress-induced apoptosis by OG was proved by decreased HSP70 and HSP72. They concluded that extracts of OG may minimize the cytotoxic effects of H_2O_2-induced Schwaan cells apoptosis by modulating the apoptotic pathway and could potentially supplement cell transplantation therapy.

Effects of *Ocimum gratissimum* on the cardiovascular system

Lahlou *et al*.[100] investigated the cardiovascular effect of intravenous administration of the essential oil of OG in rats, to ascertain whether the autonomic nervous system is involved in the mediation of OG-induced changes in mean aortic pressure (MAP) and heart rate (HR) and whether these changes could be attributed, at least in part, to the actions of eugenol, the major constituent of essential oils of OG, using both pentobarbitone-anaesthetized and conscious rats. Their results showed that intravenous administration of essential oil of OG (1-20mg/kg) or its isolate, eugenol (1-10mg/kg) to the anaesthetized and conscious rats, relicited immediate and dose-dependent decreases in MAP and HR. They reported for the first time, that intravenous administration of essential oils of OG to either anaesthetized or conscious rats induced an immediate and significant hypotension and bradycardia, which appear to be due to the actions of eugenol vasodilatory effects directly upon vascular smooth muscle.

Ofem *et al*.[101] evaluated the effect of high and low doses of leaf extracts of OG on hematological parameters in rats. Their results indicated a higher red blood cell (RBC) counts, packed cell volume (PCV), hemoglobin (Hb), and platelet counts in the high dose group compared with the control and low dose groups, with no significant changes in the total white blood cell (WBC) count in all three groups. They concluded that, oral administration of OG increases blood parameters as such may improve blood cells homeostasis.

Irondi *et al*.[102] evaluated the phenolic composition and inhibitory effect of leaves extracts of *Ocimum basilicum* and *Ocimum gratissimum* on two key enzymes, pancreatic lipase (PL) and angiotensin 1-converting enzyme (ACE) involved in obesity and hypertension, *invitro*. Their results showed that the extracts of both plants inhibited PL and ACE, and scavenged DPPH in a dose-dependent manner, with OG extract being more potent in inhibiting PL and ACE than *Ocimum basilicum*. They concluded that *Ocimum basilicum* and OG leaves

could be used as functional foods for the management of obesity and obesity-related hypertension, with OG being more effective than *Ocimum basilicum*.

Effects of *Ocimum gratissimum* on the Reproductive system

Joseph *et al*.[103] investigated the effects of methanol and oil extracts of OG on testicular morphology and epididymal sperm reserve in Wistar rats. Their results revealed no significant difference in serum testosterone level, sperm volume, livability and abnormalities, testicular biometry and testicular morphology but there was significant difference in the sperm motility and concentration. They concluded that methanol and oil extracts of OG did not have any inhibitory effect on the reproductive function and fertility of adult male albino rats.

Chao *et al*.[104] evaluated the effects of extracts of OG in preventing obesity by using ovariectomized (OVX) animal models to mimic menopausal women, as menopausal transition in women initiates with declining estrogen levels followed by significant changes in their physiological characteristics. Their results revealed significantly reduced body weight gain and adipocyte in OVX rats and showed insignificant changes in uterus weight. Further investigation indicated that extracts of OG exerted no influence on levels of dorsal fat, serum total cholesterol, and serum triacylglycerol and on serum biochemical factors, calcium, phosphorus, and glucose. They concluded that extracts of OG dietary supplements may be useful in controlling body weight of menopausal women.

Nephroprotective effects of *Ocimum gratissimum*

Ogundipe *et al*.[105] investigated the effects of aqueous extract of OG leaf on some markers of renal function in rats with gentamicin-induced nephropathy. In the experiment, markers of renal function such as creatinine, urea and total protein were determined both in the plasma and urine. Oxidative stress markers such as lipid peroxidation and GSH were assayed in the kidney tissue homogenate. Creatinine clearance was calculated using a standard formula. Their results showed significantly increased urine output, plasma urea, plasma creatinine, urinary protein, relative kidney weight and malondialdehyde (MDA), a by-product of lipid peroxidation in the gentamicin-treated group only when compared to the control group, and significantly decreased urine creatinine and GSH were also associated with gentamicin administration. Administration of aqueous extracts of OG significantly increased urine creatinine and GSH, and significantly decreased urine output, plasma creatinine, urea, MDA and urine total protein in the treated groups when compared with the gentamicin-treated group only. Histologically, they reported decreased cellularity in the glomeruli, loss of cellular constituents of tubules, densely eosinophilic (colloid) cast in the lumen of some tubules resulting in atrophy, loss of epithelial cells and severe cloudy swelling/inflammation of the distal convoluted tubules in the gentamicin-treated group only compared with the control and other groups. The results of their study indicated that aqueous extract of OG ameliorated the kidney injury caused by gentamicin in rats and concluded that extracts of OG have the potential of being used for the management of gentamicin-induced nephropathies.

Toxicity of *Ocimum gratissimum*

Ocimum gratissimum may be useful in culinary dishes and in the treatment of certain ailments but systemic toxicity is also possible and this is dose dependent. Adams et al.[106] (2008) reported on the toxicity and phytochemical constituents of aqueous extract of OG leaf and revealed several reducing sugar, tannins, saponins, cardiac glycosides, terpenes, steroids, flavonoid and alkaloids. Their histological findings in the kidneys showed acute tubular necrosis in the cortex and mononuclear cellular infiltration into the areas, In the lungs, they reported interstitial pneumonia characterized by the presence of inflammatory oedema and macrophages in the alveolar lumen coupled with thickening of the alveolar septae by congestion and exudation, necrosis and desquamation of the bronchiole epithelium and the bronchiole contained necrotic debris, the peri-bronchiolar area was densly infiltrated with macrophages and lymphocytes that were focally arranged. In the liver, they reported haemorrhages, focal areas of necrosis, mononuclear cellular infiltration and hepatocytes undergoing vacuolar changes.

Orafidiya *et al*.[107] reported that *Ocimum* oil is capable of invoking an inflammatory response that transits from acute to chronic on persistent administration, as such has toxic potentialities that should not be overlooked. Research has shown that extracts of OG affects macrophage functions and can be hepatocarcinogenic.[108] The toxicological effects of OG on the hematopoietic system showed that it caused reductions in the PCV and Hb concentration, with proliferation of leucocytes.[109-111]

Adejoke *et al*.[112] reported the nephrotoxic effects of OG, evidenced by vascular congestion, unremarkedable appearance of the interstitial spaces and glomeruli with varying degrees of interstitial infiltration by inflammatory cells. Ebeye *et al*.[113] studied the histological and biochemical effects of aqueous extract of OG leaves on the liver and kidney of adult Wistar rats. Their results showed peri-portal inflammatory cell infiltrates and central vein vascular congestion in the liver, and mild to severe intestitial infiltration by inflammatory cells and increased vascular congestion in the kidney. Ebeye *et al*.[113] reported that saponin, one of the phytochemical constituents of OG is known to be toxic to the body system and causes vascular congestion.

Udoha *et al*.[114] investigated the effect on of extracts of OG leaves on the histology of the gastrointestinal tract in

rats. Their results revealed at high dose (800 mg/kg), severe necrosis of the villi and significant erosions of the mucosa and submucosa and concluded that leaf extracts of OG although, rich in bioactive compounds and may be well tolerated at low to moderate doses during short term treatment but may cause gastrointestinal toxicity when used continuously over a long period.

Shittu *et al*.[115] investigated the testiculotoxic effects of OG on sperm quality and testicular morphology in alloxan-induced diabetic rats. Their results showed increased abnormal sperm cells, mild vacuolation in the seminiferous tubule, disorganized germinal cells layer, arrested sperm maturation with empty spermatozoa in lumen, decreased seminiferous tubule diameter and increased interstitial space in the testes of OG, diabetic and diabetic+OG-treated rats compared with control. They concluded that diabetes induced sperm impairments and distortions in testicular cytoarchitecture, which were aggravated by OG leaf extract in male Wistar rats.

Obianime *et al*.[116] investigated the effects of aqueous leaf extract of OG on hormonal and semen parameters of mice. Their results showed that OG decreased sperm count and motility were decreased, while the percentages of abnormal sperm cells, sperm debris and primordial cells were increased dose- and time-dependently. Histologically, OG caused damages to the seminiferous epithelium, characterized by varying degrees of edema within the tubules and the interstitial cells, reduced spermatogenesis (maturation arrest) and collapse of the tubules under the tunica albunigea. They concluded that OG exhibited anti-fertility activity in the male mouse, which may have been mediated through a direct deleterious action on the testis without disruption of the testicular endocrine function.

Parandin and Haeri Rohani[117] investigated the effect of the oil extract of OG leaves on the reproductive function and fertility of adult male rats. Their results revealed significant decrease in the gonado-somatic index, sperm motility, sperm viability, epididymal sperm reserve and daily sperm production, level of testosterone in the serum and fertility percentage after days of treatment of rats with high dose oil extracts of OG, and oil extracts of OG leaves at dose (300 mg/kg) had a negative impact on the male reproductive function and fertility.

Okigbo and Ogbonnaya[44] tested the bioactivities of OG on the insect pest sitophilus zeamais, a major pest of stored maize. The insecticidal activity was tested by putting 20 adult representatives of S. zeamais with 20g of maize grains powdered with various mixtures of essential oil and Kaolin (5 and 10%). The tested essential oils of OG protected 74% of the test-material against the S. zeamais population after 4 days. A direct application of the OG on the test insects was found to be 85.7% by knock down effect.

CONCLUSION

The extracts and essential oils obtained from *Ocimum gratissimum* have gained much appreciation among food scientists and researchers because of their multifold biological activities. *Ocimum gratissimum*, a natural medicinal plant with much potential benefits and less toxic constituents, is useful in culinary dishes and in the treatment of certain ailments, however, systemic toxicity is also possible which have been seen to be dose dependent. Hence, caution should therefore be exercised in the therapeutic use of the plant. This reviewed article will lend credence to scientists and researchers interested in the formulation of new drugs and supplements from natural plant products as well as those investigating the pharmaceutical diversity of essential oils, with a view of contributing a lot to solving certain economic and health problems. Bearing all of the above in mind, it is hopeful that the essential oils and their constituents of *Ocimum gratissimum* can be considered in the near future for more clinical evaluations and applications.

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